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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769,420	01/26/2001	Sui Xiong Cai	1735.0440001/RWE/BEC	4240

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W., SUITE 600
WASHINGTON, DC 20005-3934

EXAMINER
MCKENZIE, THOMAS C

ART UNIT	PAPER NUMBER
1624	4

DATE MAILED: 01/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/769,420	CAI ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-73* is/are pending in the application.

4a) Of the above claim(s) *5-27,30,31,49,52,62-70,72 and 73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,28,29,32-48,53-61 and 71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2&3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. This action is in response to an application filed on 1/26/01. There are seventy-three claims pending and thirty-five under consideration. Claims 58-61 are compound claims. Claim 71 is a composition claim. Claims 1-4, 28, 29, 32-48, and 51-57 are use claims. This is the first action on the merits. The application concerns some nicotinamide compounds, compositions, and uses thereof.

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 58-61, 32-41, and parts of 1-4, 28, 29, 42-48, 51-57, and 71, drawn to nicotinamides, compounds of Formula (III) classified in class 546, subclass 316, among others.

II. Claims 62-65, 20-23, and parts of claims 1-4, 42-48, 51-57, and 71, drawn to pyrazine amides, compounds of Formula (VI), classified in class 544, subclass 406, among others.

III. Claims 66-69, 15-19, and parts of claim 1, 2, 4, 42-48, 51-57, and 71, drawn to benzamido pyridines, compounds of Formula (VII), classified in class 546, subclass 309, among others.

IV. Claim 5-14, 24-27, 30, 31, 51, 52, 70, and parts of claims 1-4, 28, 29, 42-48, 51-57, and 71, drawn to heterocyclic carboxamides of Formula (V) and uses thereof, classified in class 544, subclass 2, among others.

V. Claims 49, 50, 72, and 73, drawn to complex compositions, classified in class 514, subclass 1, among others.

If Applicants chose Group IV, then additional restriction will be required.

If applicants elect group V, the complex compositions, then they must also elect a species of chemotherapeutic for purposes of classification and examination.

Claim 1, 2, 4, 42-48, 51-57, and 71 links Groups I-IV.

Claim 3 links Groups I, II, and IV.

Claims 28 and 29 link Groups I and IV.

3. The inventions are distinct, each from the other because of the following reasons: These multiple claimed heteroaryl rings are chemically non-equivalent and are not art-recognized as sharing the same biological properties. Inventions I-IV have acquired a separate status in the art as shown by their different classification, thus the patent search required for Group I is not co-extensive with that required for Groups II-IV. The basic names of these heterocycles differ, thus the literature search for these various species will be divergent. Because these inventions are distinct for the reasons given above, restriction for examination purposes as indicated is proper.

Inventions V and I-IV are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the

combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the additional chemotherapeutic agents have utility against cancer without Applicants additional compounds. The subcombinations I-IV have separate claimed utility such as treatment of arthritis distinct from chemotherapy. Simple compositions and those with an additional active ingredient are patentably distinct because the combination (complex composition) can be patentable even if the subcombinations (the individual compounds) are not. This is because of the possibility of synergistic interaction, which is usually the purpose of the complex composition in the first place. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the search required for Group I-IV is not required for Group V, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Bruce Chalker on 1/8/02 a provisional election was made without traverse to prosecute the invention of Group I, claims 58-61, 32-41, and parts of 1-4, 28, 29, 42-48, 51-57, and 71. Applicant in replying to this Office action must make affirmation of this election. Claims 5-27, 30, 31,

49-52, 62-70, 72, and 73 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

6. Claims 1-4, 28, 29, 42-48, 51-57, and 71 are rejected on the grounds as being drawn to an improper Markush group *In re Harnisch* 206 USPQ 300. The claimed compositions and methods that employ them present a variable core. Formula (V) contains compounds drawn to the non-elected inventions, with Ar' other than 3-pyridyl.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 28, 29, and 32-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrases "a disorder

responsive to the induction of apoptosis" and "a mammal in need of such treatment" are indefinite. The claims provide for the use of the compounds of formula V, but the claims do not set forth any steps involved in determining how to identify what disorders or mammals are to be treated. It is unclear what diseases and treatments applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how to practice this use. Identifying which diseases applicants intend this claim to cover will involve extensive and potentially inconclusive clinical research. With out such clinical research to identify the patients and diseases applicants intend to treat, one skilled in the art cannot determine the metes and bounds of the claim. Hence, the claims are indefinite.

8. Claims 1-4, 28, 29, 32-38, 40, 42-48, 51-57, 58, 60, and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The word "prodrug", which occurs in claims 1, 2, 33, 40, 42, 43, 46, 47, 58, and 60 is indefinite. The issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' "prodrugs" are molecules whose structure lie outside the subject matter of claim 1, but upon metabolism in the body are converted to active compounds falling within

the structural scope of claim 1. The claim describes the function intended but provides no specific structural guidance to what constitutes a "prodrug". Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claim 1. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise.

9. Claims 1-4, 28, 29, 32-38, 40, 42-48, 53-57, 58, 60, and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrases "optionally substituted aryl", optionally substituted heteroaryl" "Ar' is optionally substituted" etc, which occurs in claims 1, 2, 4, 28, 29, 32, 33, 34, 42-44, and 46-48, are indefinite. Optionally substituted by what?

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 28, 29, and 32-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. The how to use

portion of the statute means that Applicants must teach the skilled practitioner, in this case a physician, how to treat the claimed disease. The physician clearly must know what disease and what symptoms she is to treat.

11. Claims 1-4, 28, 29, 32-41, 42-48, 51-57, 58-61, and 71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As discussed by Testa (Burger's Medicinal Chemistry, 5ed, Chapter 6), the nitro aryl functional group is a toxophoric group. The table spanning both columns of page 177 lists eight suspect groups but only three, acetylenes, aromatic nitro compounds, and thiols lack the qualifier "some" indicating these three are most problematic. The reason for the concerning regarding the toxicity of nitro aryl functional groups is provided by Low (Burger's Medicinal Chemistry, 4ed, Chapter 3) who states in the second paragraph on page 175, that such compounds are reduced enzymatically in the liver and produce highly carcinogenic hydroxylamines.

Since Applicants' intended use of their compounds is as pharmaceutical agents, the likelihood of toxicity means the skilled clinician would not know how to use Applicants' compound for their intended purpose. The USPTO Board of

Patent Appeals and Interferences held in *Ex parte Jovanovics* 211 USPQ 907 while Applicants "need not prove absolute safety or effectiveness", that "[t]he courts have held that, when a reasonable doubt exists, concerning the operability of a claimed invention, it is appropriate for an examiner to request a showing to resolve the doubt. *In re Ruskin*, 53 CCPA 872, 354 F. 2d 395, 148 USPQ 221; *In re Novak*, 49 CCPA 1283, 306 F. 2d 924, 134 USPQ 335. Since appellants' allegation that effective treatment of particular cancers in humans may be achieved with their new compounds is not entirely believable on its face, we believe that the examiner was justified in challenging the correctness of appellants' asserted utility."

12. Claims 1-4, 28, 42-48, and 51-57 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Ar = phenyl, does not reasonably provide enablement for Ar = aryl generally or heteroaryl. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification is not adequately enabled for the scope of ring Ar other than phenyl. Compounds made and tested represent the scope of claim 29, not claim 1. There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (V) will all share the same

biological properties. The diverse claimed fused aryl and heteroaryl rings are chemically non-equivalent and there is no basis in the prior art for assuming in the non-predictable art of pharmacology that structurally dissimilar compounds will have such activity, *In re Surrey* 151 USPQ 724.

13. Claims 42-48, 51, and 52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants are not enabled for "treating or preventing cancer" generally. There are two issues here. Firstly, Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689.

To make clearer the lack of enablement for treatment of all cancer, extrinsic evidence is supplied by Draetta (Ann. Reports Med. Chem.), final sentence on page 246 "Although many still think about the need for a magic bullet as a cure for all cancers, our knowledge of the molecular mechanism underlying this disease make the prospect of developing such a universal cure very unlikely." Since no universal cure for cancer has been developed, it follows that there is no correlation

between the assays relied upon by applicants and the ability to treat all cancers. Thus, those assays are not sufficient to enable such claims.

The remarkable advances in chemotherapy have seen the development of specific compounds to treat specific types of cancer. The great diversity of diseases falling within the "tumor" category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task.

14. Secondly, Applicants are not enabled for preventing any disease. The only established prophylactics are vaccines not the nicotinamide analogs such as present here. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of respiratory diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo*

Nordisk, 42 USPQ2nd 1001, 1006. The Examiner suggests deletion of the word "prevention".

15. Claim 53 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The treatment of "autoimmune diseases" generally would be unprecedented feat. For a compound or genus to be effective against "autoimmune diseases" generally is contrary to medical science. The "autoimmune diseases" are a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There are hundreds of such diseases, which have fundamentally different mechanisms and different underlying causes. There are both chromic and acute "autoimmune diseases", most of which lack satisfactory treatment. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving

such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006.

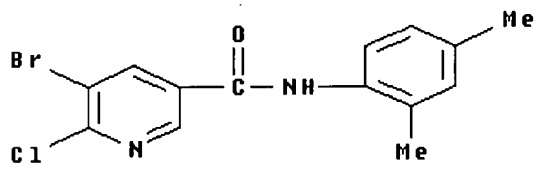
16. Claim 56 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of "skin disease" cannot be deemed enabled. The term "skin disease" covers a broad array of different disorders that have different modes of action and different origins. The term would embrace such unrelated disorders as sun burn, acne, and melanoma. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609.

Claim Rejections - 35 USC § 102

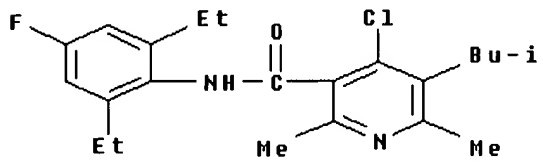
17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claim 58 is rejected under 35 U.S.C. 102(b) as being anticipated by Setliff (Proc. Arkansas Acad. Sci.). The compound shown below fits Formula III with $R_1 = R_3 =$ methyl, $R_2 = R_4 = R_5 = R_6 = R_7 = R_{11}$ = hydrogen, R_9 = chlorine, and R_{10} = bromine. Since the reference is not readily available, an abstract is being furnished.



18. Claims 58 and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by Yagihara ('385). There are two compounds in this reference which anticipated Applicants compound and composition claims. The compound shown below fits Formula III with $R_1 = R_5$ = ethyl, R_3 = fluorine, $R_2 = R_4 = R_{11}$ = hydrogen, R_6 = chlorine, $R_7 = R_9$ = methyl, and R_{10} = isobutyl. The compounds are found in Table 1, columns 13 and 14 and are compounds 42 and 46. Additional 5-alkyl pyridinecarboxamides are listed in columns 5-11.



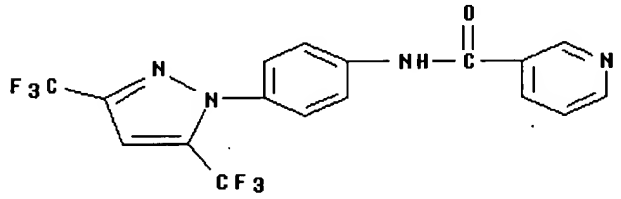
19. Claims 1-4, 28, 29, 32, 42-48, 53, 54, 56, and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Gammill ('075). Compound 16 of the reference anticipated Applicants' use claims and fits formula (V) with Ar' = 3-pyridyl and Ar = 2-(4-morpholinyl)-4H-benzopyran-4-0n-6-yl. The compound is found in lines 54-55, column 20. Activity against cancer, arthritis, and psoriasis is disclosed in in lines 11-24, column 16.

20. Claims 1-4, 28, 29, 32, 53, and 55-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Okamoto ('519). Compound 8 anticipated Applicants' use claims and fits formula (V) with Ar' = 3-pyridyl and Ar = 6-methoxy-4,5,7-trimethylbenzothiaz-2-yl. The compound is found in Example 8, lines 31-55, column 21. Activity against psoriasis is taugh in line 38, column 17. Activity againsy inflammatory bowel disease is claimed in claim 17.

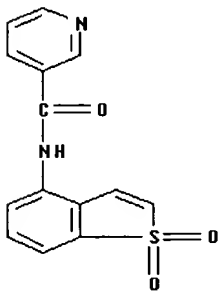
21. Claims 1-4, 28, 29, 32, 53, and 55-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Clemence (FR 2,636,329 A2). One compound of this reference anticipated Applicants' use claims and fit formula (V) with Ar' = substituted 3-pyridyl and Ar = thiaz-2-yl. Activity against psoriasis is taugh in line 38, column 17. Activity against autoimmune diseases and rhematoid arhtritis is taught in lines 22-25, page 8.

22. Claims 1-4, 28, 29, 32, 53, and 54 are rejected under 35 U.S.C. 102(a) as being anticipated by Oku, (JP 10291988 A2). There are sixty compounds of this reference which anticipated Applicants' use claims and fit formula (V) with Ar' = substituted 3-pyridyl and Ar = substituted quinolyl Activity against rhematoid arthritis is taught in the abstract. Since no English traslation of this reference is available, an abstract is being furnished.

23. Claims 1-4, 28, 29, 32, 33, 36, 38, 53, and 54 are rejected under 35 U.S.C. 102(a) as being anticipated by Kubotab (WO 9919303 A1). There is one compound in this reference, which anticipates Applicants' use claims. The compound is shown below and fits formula (V) with Ar' = 3-pyridyl and Ar = 4-[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl]phenyl with R_3 = 3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl. Activity against autoimmune diseases and rheumatoid arthritis is taught in the abstract. Since no English traslation of this reference is available, an abstract is being furnished.

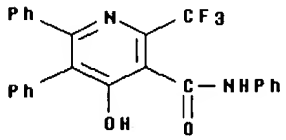


24. Claims 1-4, 28, 29, 32-36, 42-48, 53, 54, 56, and 57 are rejected under 35 U.S.C. 102(a) as being anticipated by Konishi (WO 9951587 A1). There are five compounds in the reference, which anticipate Applicants' use claims including the one shown below. The compound is shown below and fits formula (V) with Ar' = 3-pyridyl and Ar = 1,1-dioxidobenzo[b]thien-4-yl, with $R_1 = R_2$ = thienyl. Activity against multiple myeloma, plasma cell leukemia, psoriasis, renal cell cancer, chronic rheumatoid arthritis, and autoimmune diseases, is taught in the abstract. Since no English traslation of this reference is available, an abstract is being furnished.

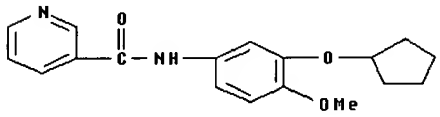


25. Claims 1-4, 28, 29, 32, 33, 53, and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Clemence ('140). There is one compound in this reference, which anticipates Applicants' use claims. The compound is shown below and fits formula (V) with Ar' = 4-hydroxy-5,6-diphenyl-2-(trifluoromethyl)-3-pyridyl, with R_6 = hydroxy, R_7 = trifluoromethyl, $R_9 = R_{10}$ = phenyl and Ar = phenyl. It is

Example 4, lines 13, column 10 to line 43, column 11. Activity against rheumatoid arthritis is taught in claim 15 of the reference.

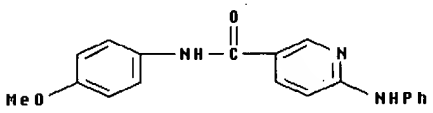


26. Claims 1-4, 28, 29, 32, 33, 36, 56, and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Beeley ('827). There is one compound in this reference, which anticipates Applicants' use claims. The compound is shown below and fits formula (V) with Ar' = 3-pyridyl and Ar = 3-(cyclopentyloxy)-4-methoxyphenyl with R_3 = methoxy and R_4 = cyclopentyloxy. It is Example 7, lines 11-19, column 10. Activity against psoriasis is taught in line 32, column 5.



27. Claims 1-4, 28, 29, 32, 33, 36, 42-48, and 53-57 are rejected under 35 U.S.C. 102(e) as being anticipated by Mantlo ('884). There are over one hundred compounds disclosed in this reference, which anticipate Applicants' use claims. One compound is shown below and fits formula (V) with Ar' = 6-(phenylamino)-3-pyridyl with R_9 = phenylamino and Ar = 4-methoxyphenyl with R_3 = methoxy. The compounds are found in Tables 8-13, spanning columns 84-91. See also

compound claims 1-15 in this reference. Activity against rheumatoid arthritis is taught in line 36, column 96 of the reference. Activity against inflammatory bowel disease and psoriasis is taught in line 40-41, column 96. Activity against cancer is taught in line 57, column 96.



Conclusion

28. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for before final amendments is (703) 872-9306. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

Mukund J. Shah

Mukund Shah
Supervisory Patent Examiner
Art Unit 1624

TCMcK
January 10, 2002